AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph beginning on page 18, line 37, as follows:

Among the aptamers described above, some have a common structure, defined by formula II below:

5'$R_4X_6X_5X_4X_3$GGAAUAG$X_2X_1R_3X'_1X'_2$CGUAUAC$X'_3X'_4X'_5X'_6R_5$ 3' (SEQ ID NO: 34)

(II), the secondary structure of which is represented in figure 10, and in which:

- the riboses of the purines bear an OH group in the 2'-position and the riboses of the pyrimidines bear a fluorine atom in the 2'-position,
- **R_3** is present or absent and represents an apical bulge (or loop) comprising:
  - a linear or branched carbon chain selected from the group consisting of C_6-C_{30} alkyl groups or C_6-C_{30} aryl groups;
  - a polymer such as PEG or PEI, or the like;
  - functional groups such as biotin, streptavidin, peroxidase, etc.;
  - other molecules of interest such as, for example, active ingredients, labeling tags, in particular fluorescent tags, or chelating agents for radioisotopes;
  - a natural (DNA or RNA) or modified nucleotide sequence (for example: 2'-fluoro, 2'-O-methyl, PNA, LNA, etc.); preferably, R_3 represents the following bulges or loops (1) to (4):

    loop (1): 5' UGGAAGGA 3' (SEQ ID NO:29)

    loop (2): 5' CUUUUUU 3' (SEQ ID NO:30)

    loop (3): 5' GNPuA 3'

    loop (4): 5' UNCG 3',

    in which the riboses of the purines bear a hydroxyl function on the carbon in the 2'-position, while the riboses of the pyrimidines bear a fluorine atom on the carbon in the 2'-position,

- **X_1, X'_1, X_2, X'_2, X_3, X'_3, X_4, X'_4, X_5, X'_5, X_6 and X'_6** represent Py or Pu with, preferably:

  X_1-X'_1 corresponding to C-G, A-U, G-C or U-A

  X_2-X'_2 corresponding to C-G, A-U, G-C or U-A

  X_3-X'_3 corresponding to C-G, A-U, G-C or U-A

  X_4-X'_4 corresponding to C-G, A-U, G-C or U-A

  X_5-X'_5 corresponding to C-G, A-U, G-C or U-A

  X_6-X'_6 corresponding to C-G, A-U, G-C or U-A

  N corresponding to G or C or A or U,

  Pu corresponding to G or A, in which the riboses bear an OH group in the 2'-position (natural RNA chemistry),

  Py corresponds to U or C, in which the riboses bear a fluorine atom in the 2'-position, and

- **R_4** and **R_5** are present or absent and represent:

. a natural (DNA or RNA) or modified nucleotide sequence (for example: 2'-fluoro, 2'-O-methyl, PNA, LNA, etc.), comprising between 1 and several thousand nucleotides, preferably between 1 and 39 nucleotides; a part of said nucleotide sequence or said sequence preferably comprising one of the following sequences:

  R_4 :

  5'-R_1-Z_1-3', with Z_1=G: 5' GGGAGACAAGAAUAAACGCUCAAG 3' (SEQ ID NO:18)

  or

  5'-R_1-Z_1-3', with Z_1=GCGGUAU (SEQ ID NO:26):

  5' GGGAGACAAGAAUAAACGCUCAAGCGGUAU (SEQ ID NO:19), and

  R_5 :

  5'-Z_2-R_2-3', with Z_2=CAAUCCAGGGCAACG (SEQ ID NO:27):

5' CAAUCCAGGGCAACGAACGACAGGAGGCUCACAACAGGA 3' (SEQ ID NO:20) or

5'-Z_2-R_2-3', with Z_2=ACCGCAGCG (SEQ ID NO:28):

5' ACCGCAGCGAACGACAGGAGGCUCACAACAGGA 3' (SEQ ID NO:21),

- a linear or branched carbon chain selected from the group consisting of C_6-C_{30} alkyl groups or C_6-C_{30} aryl groups;
- a polymer such as PEG or PEI, or the like,
- functional groups such as biotin, streptavidin, peroxidase, etc.,
- other molecules of interest such as, for example, active ingredients, labeling tags, in particular fluorescent tags, or chelating agents for radioisotopes.

Please amend the paragraph beginning on page 21, line 23, as follows:

- When R_3 represents 5' CUUUUUU 3' (SEQ ID NO:30: loop (2)), 5'GNPuA 3' (loop 3) or 5'UNCG 3'(loop 4), R_4 comprises from 1 to 30 nucleotides selected from SEQ ID NO:19 or from 1 to 24 nucleotides selected from SEQ ID NO:18 and R_5 comprises from 1 to 33 nucleotides selected from SEQ ID NO:21 or from 1 to 39 nucleotides selected from SEQ ID NO:20, the aptamer exhibiting such a structure has only properties of binding to said Ret receptor in its activated form, and in particular to the Ret receptor mutated in its extracellular domain. When R_3 represents 5' CUUUUUU 3' (SEQ ID NO: 30) (loop 2), R_4 represents SEQ ID NO:19 and R_5 represents SEQ ID NO:21, the secondary structure of this product is represented in figure 12; the preferred product is represented by SEQ ID NO:25 and belongs to the family D24, in which R_4 and R_5 comprise at least one nucleotide. This aptamer comprises successively from 5' to 3': SEQ ID NO:1 + SEQ ID NO:7 + SEQ ID NO:2, with reference to formula I.

Please amend the paragraph beginning on page 22, line 3, as follows:

- When R_3 represents 5' UGGAAGGA 3' (SEQ ID NO: 29) (loop 1), and in the absence of R_4 and of R_5, the aptamer exhibiting such a structure has only properties of binding to said Ret receptor in its activated form. A preferred aptamer corresponding to the latter definition corresponds to a part of SEQ ID NO:3 of family D4 (SEQ ID NO:23).

Please amend the paragraph beginning on page 23, line 33, as follows:

According to an advantageous embodiment of said reagent, it corresponds to an aptamer of formula II, as defined above:

5'$R_4X_6X_5X_4X_3$GGAAUAG$X_2X_1R_3X'_1X'_2$CGUAUAC$X'_3X'_4X'_5X'_6R_5$3' (SEQ ID NO: 35), in which R_3, R_4 and R_5 are absent.

Please amend the paragraph beginning on page 24, line 7, as follows:

According to another advantageous embodiment of said reagent, it corresponds to an aptamer of formula II, in which R_3 represents 5' CUUUUUU 3' (SEQ ID NO: 30) (loop (2)), R_4 represents the sequence SEQ ID NO:19 and R_5 represents the sequence SEQ ID NO:21; this aptamer corresponds to SEQ ID NO:25, and comprises successively from 5' to 3', with reference to formula I: SEQ ID NO:1 + SEQ ID NO:7 + SEQ ID NO:2, as specified above.

Please amend the paragraph beginning on page 27, line 30, as follows:

- Figure 5 (A): comparison of the prediction of the secondary structure of the D4 (SEQ ID NO: 3) and D24 (SEQ ID NO: 7) aptamers. The secondary structure prediction is carried out using the **RNAstructure** software written by David H. Mathews, http://rna.chem.rochester.edu. The algorithm is based on the searches described in D.H. Mathews et al. (Journal of Molecular Biology, 1999, 288, 911-940, mentioned above).

Please amend the paragraph beginning on page 30, line 7, as follows:

- Figures 10 to 15: secondary structure of the following aptamers: formula II (SEQ ID NO: 34) (figure 10); D4 (SEQ ID NO: 22) (figure 11); D24 (SEQ ID NO: 25) (figure 12); D30 (SEQ ID NO: 31) (figure 13); D12 (SEQ ID NO: 32) (figure 14) and D71 (SEQ ID NO: 33) (figure 15).

Please amend the paragraph beginning on page 31, line 11, as follows:

1. Before selection, by PCR amplification of the DNA sequence:

B2S0: 5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCC3' (SEQ ID NO: 36) where N represents a random sequence of 50 nucleotides

1st PCR cycle:

* *Hybridization* (SEQ ID NOS 36 and 16, respectively, in order of appearance)

```
5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCC3' (B2S0)
 (primer P10)            3'AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'
(SEQ ID NO:16)
```

* *Elongation* (SEQ ID NOS 37-38, respectively, in order of appearance)

```
5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCCTATAGTGAGTCGTATTA3'
3'AGGACAACACTCGGAGGACAGCAA-M-AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5',
```

where the text in bold represents the polymerized sequence and M represents the sequence complementary to N.

2nd PCR cycle:

* *Denaturation* (SEQ ID NOS 37-38, respectively, in order of appearance)

```
5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCCTATAGTGAGTCGTATTA3'
3'AGGACAACACTCGGAGGACAGCAA-M-AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'
```

* *Hybridization* (SEQ ID NOS 37, 16-17, and 38, respectively, in order of appearance)

```
5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCCTATAGTGAGTCGTATTA3'
                              3'AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'
(primer  P10:  SEQ ID NO:16)


5'TCCTGTTGTGAGCCTCCTGTCGTT3'   (primer P30 : SEQ ID NO :17)
3'AGGACAACACTCGGAGGACAGCAA-M-AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'
```

* *Elongation* (SEQ ID NOS 37-38 and 37-38, respectively, in order of appearance)

```
5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCCTATAGTGAGTCGTATTA3'
3'AGGACAACACTCGGAGGACAGCAA-M-AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'

5'TCCTGTTGTGAGCCTCCTGTCGTT-N-TTGAGCGTTTATTCTTGTCTCCCTATAGTGAGTCGTATTA3'
3'AGGACAACACTCGGAGGACAGCAA-M-AACTCGCAAATAAGAACAGAGGGATATCACTCAGCATAAT5'
```

the text in bold representing the polymerized sequence and M represents the sequence complementary to N.

Please amend the paragraph beginning on page 32, line 10, as follows:

2. During selection, by RT-PCR amplification of the selected 2'-F-Py RNAs, of formula R_1-R-R_2, as defined above:

5'GGGAGACAAGAAUAAACGCUCAA-R-AACGACAGGAGGCUCACAACAGGA3' (SEQ ID NOS 1-2, respectively, in order of appearance), where R represents the sequence of the 2'-F-Py RNAs selected.

Reverse transcription (RT) (SEQ ID NOS 1-2, 17, 1-2, 39 and 17, respectively, in order of appearance)**:**

* *Hybridization*

```
5'GGGAGACAAGAAUAAACGCUCAA-R-AACGACAGGAGGCUCACAACAGGA3' (2'-F-Py RNA)
                            3'  TTGCTGTCCTCCGAGTGTTGTCCT5' (primer P30)
```

* *Elongation*

```
5'GGGAGACAAGAAUAAACGCUCAA-R-AACGACAGGAGGCUCACAACAGGA3'
3'CCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5',
```

where the text in bold represents the polymerized sequence and S represents the sequence complementary to R.

1st PCR cycle (SEQ ID NOS 39, 17, 16, 39, 17, 16, 40-41 and 17, respectively, in order of appearance):

* *Denaturation*

```
3'CCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

(cDNA of the 2'-F-Py RNA)

* *Hybridization*

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA3' (primer P10)
                  3'CCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

* *Elongation*

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

where the text in bold represents the polymerized sequence and S represents the sequence complementary to R.

2nd PCR cycle:

* Denaturation (SEQ ID NOS 16, 40-41 and 17, respectively, in order of appearance)

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'

3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

* Hybridation (SEQ ID NOS 16, 40, 17, 16, 41 and 17, respectively, in order of appearance)

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
                        (primer P30)       3'TTGCTGTCCTCCGAGTGTTGTCCT5'

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA3' (primer P10)
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

* Elongation (SEQ ID NOS 16, 40-41, 17, 16, 40-41 and 17, respectively, in order of appearance)

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
3'**ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT**-S-TTGCTGTCCTCCGAGTGTTGTCCT5'

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-**AACGACAGGAGGCTCACAACAGGA3'**
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'

where the text in bold represents the polymerized sequence and S represents the sequence complementary to R.

Please amend the paragraph beginning on page 33, line 23, as follows:

3. After selection, by PCR amplification of the aptamers from plasmid in which they have been cloned

The plasmids contain the sequence (SEQ ID NOS 16, 40-41 and 17, respectively, in order of appearance):

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-**AACGACAGGAGGCTCACAACAGGA3'**
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'

where R represents the DNA sequence specific for the aptamer and S the sequence complementary to R.

1st PCR cycle:

* *Denaturation* (SEQ ID NOS 16, 40-41 and 17, respectively, in order of appearance)

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'

3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'

* *Hybridization* (SEQ ID NOS 16, 40, 17, 16, 41 and 17, respectively, in order of appearance)

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
                    (primer P30)            3'TTGCTGTCCTCCGAGTGTTGTCCT5'

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA3'  (primer P10)
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

* *Elongation* (SEQ ID NOS 16, 40-41, 17, 16, 40-41 and 17, respectively, in order of appearance)

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'

5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

where the text in bold represents the polymerized sequence and S represents the sequence complementary to R.

Please amend the paragraph beginning on page 34, line 26, as follows:

***in vitro* transcription:**

One of the two strands of the PCR-amplified DNA serves as a template for the *in vitro* transcription of the double-stranded 2'-F-Py RNAs. The sequence underlined corresponds to the region of the T7 phage RNA polymerase promoter (SEQ ID NOS 16, 40-41, 17, 42, 40, 43-44, 41 and 17, respectively, in order of appearance).

```
5'TAATACGACTCACTATAGGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
                      /  GGGAGACAAGAATAAACGCTCAA-R-AACGACAGGAGGCTCACAACAGGA3'
5'TAATACGACTCACTATAGGGAGACAAGAAUAAACGCUCAA-R-AACGACAGGAGGCUCACAACAGGA3'
3'ATTATGCTGAGTGATATCCCTCTGTTCTTATTTGCGAGTT-S-TTGCTGTCCTCCGAGTGTTGTCCT5'
```

Please amend the paragraph beginning on page 40, line 24, as follows:

Table III: Results of the selection (the sequences are given without the fixed regions R1 (SEQ ID NO:1) and R2 (SEQ ID NO:2) which border them and allow RT-PCR amplification) (SEQ ID NOS 45, 4, 46, 14, 11, and 47-54, respectively, in order of appearance).

Sequence code (number of clones)	Sequence (R)	binding at 100 nM on PC12 MEN 2A	Kd on PC12 MEN 2A (nM)	number of targets/cell (× 1000)
D14(23)	GGCCATAGCGCACCACCAAGAGCAAATCCCTAAGCGCGACTCGAGTGAGC	-		
D12(21)	GGGCUUCAUAAGCUACACCGGCCAACGCAGAAAUGCCUUAAGCCCGAGUU	+	67 ± 7	102 ± 25
D30(7)	AGGCGAGCCCGACCACGTCAGTATGCTAGACAACAACGCCCGCGTGGTAC	+	74 ± 25	212 ± 27
D71(5)	GGCCCUUAACGCAAAAACGAAGGAUCAUCGAUUGAUCGCCUUAUGGGCU	+	53 ± 7	248 ± 42
D42(4)	GACCCGUAUGAAGGUGGCGCAGGACACGACCGUCUGCAAUGAGCGAGC	-		
D20(2)	GGGCCAATCGAAGCCGGTAATTCCCAAACTAACGTGCAAACTGCACCCGC	-		
D76	GGCTTACACGGAGAAACAAGAGAGCGGCCCAAACTTGATTGACAGTGGCC	-		
D60	CCGACCTGTACAGCAGTTAGTTACACGTTTGAAACAACCGGCGTTCGAGC	-		
D32	CCCCGCTTTTTGACGTGATCGAACGCGTATCAGTAACGTCAGCAGTCGAGC	-		
D33	CAAAGCGTGTATTCTCGTGAGCCGACCATCGTTGCGAACATCCCCGGAACG	-		
D87	CCGCGGTCTGTGGGACCCTTCAGGATGAAGCGGCAACCCATGCGGGCC	-		
D24	GCGGTATGTAGGGAATAGCACTTTTTTTGCGTATACCTACACCGCAGCG	+	32 ± 5	102 ± 58
D4	GCGCGGGAATAGTATGGAAGGATACGTATACCGTGCAATCCAGGGCAACG	+	35 ± 3	110 ± 47

Please replace the originally filed Sequence Listing with the attached Substitute Sequence Listing beginning on new page 62.